REMARKS

This is a response to the Office Action dated June 12, 2009 (hereinafter "Office Action"). Claims 1-141 and 154-156 were previously canceled. Claims 142 and 159 have been amended to remove repetitive language from the claims. Upon entry of this amendment, claims 142-153 and 157-164 will be pending. No new matter had been made as a result of the amendment.

I. Priority

The Examiner has objected to the presentation of the benefit of priority claim to U.S. Patent Application No. 08/338,501, filed on November 22, 1994. As recommended by the Examiner the chain of priority has been amended to specify that U.S. Patent Application No. 08/338,501 claims priority to PCT/SE93/00455 filed on May 21, 1993 by virtue of being a 371 national stage application of PCT/SE93/00455 filed on May 21, 1993. As a result of this amendment, the priority chain conforms to the benefit of priority claim presented in the corrected filing receipt of U.S. Patent Application No. 09/549,642 that was issued on June 22, 2009, a copy of which is enclosed herewith. It is considered that these corrections overcome the remaining formal objections to the priority claim and thus withdrawal of the objections is requested.

II. The Prior Art Rejections

1. The 35 U.S.C. § 102(b) Rejection over Lindblom

Claims 142-149 and 150-153 and 157-164 have been rejected under 35 U.S.C. §§102(b) and/or 103(a) over WO 93/24142 (hereinafter Lindblom), which is the publication of International Patent Application no. PCT/SE93/00455 filed on May 21, 1993.

In view of the corrections to the claims for benefit in the present specification and the filing receipts of the present application and parent application no. 09/549,642, the present application should be granted the benefit of priority to PCT/SE93/00455 (See Office Action, page 3, paragraph 5). As a result, Lindblom cannot be considered as prior art against the present application. Applicant therefore respectfully requests that the rejections over Lindblom be withdrawn.

2. The 35 U.S.C. § 103(a) Rejection over Ractliff in view of Hellgren and Karlstam

Claims 142-150 and 157-164 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent no. 4,837,009 (Ractliff), in view of U.S. Patent no. 4,963,491 (Hellgren) and EP 0 257 003 (Karlstam). This rejection is traversed and reconsideration is requested for the reasons given below.

Ractliff discloses a method for the prevention of plaque formation using chlorine dioxide to oxidize the sulphide bonds in sulphated glycoproteins which are involved in the first step of the formation of plaque on a clean tooth surface (See Ractliff col. 3, lines 51-55). As a result, pellicle formation is inhibited and bacterial adhesion and subsequent steps in plaque formation are retarded (See Ractliff col. 3, lines 55-59). Ractliff, however, fails to teach a method for removing dental plaque since Ractliff is only concerned with preventing the formation of plaque in the first place. Furthermore, Ractliff expressly states that, "[n]o disulphate enzymes capable of cleaning the sulphate moieties of glycoproteins are known" (See Ractliff, col. 3, lines 59-61). Furthermore, Ractliff also fails to teach a composition including enzymes isolated from krill, as required by claims 142 and 159.

The Examiner instead relies on Hellgren to teach a method for cleaning teeth using krill derived enzymes (See Hellgren col. 1, line 31). Hellgren, however, only addresses the use of specific exo- and endo-peptidases derived from krill (See Hellgren col. 1, line 31). Additionally, the Examiner has acknowledged that "[Hellgren] does not teach or suggest that the composition may be used to treat or remove dental plaque" (See page 8 of the Office Action dated January 17, 2008).

The Examiner also relies on the statement in Karlstam that krill derived enzymes degrade a particular glycosoaminoglycan, i.e. hyaluronic acid. Karlstam, however, only teaches that Antarctic krill contains hyaluronidase which has endo-gluconidase-like activity, i.e. cleaves the glucoronic acid linkages of hyaluronic acid (See Karlstam page 2, lines 29-32; page 3, lines 5-6). Furthermore, the Examiner has recognized that [Karlstam] does not teach the use of the enzyme to degrade plaque" (See page 8 of the Office Action dated January 17, 2008).

i. The cited references do not teach a method for removing plaque

Ractliff does not teach or suggest any method for removing plaque, as required by independent claims 142 and 159. Rather, Ractliff is solely directed to the prevention or inhibition of plaque formation by oxidizing sulphide bonds in sulphated glycoproteins, which are involved in the first step of plaque formation. While Ractliff repeatedly teaches that its method is intended to "effectively inhibit the initial pellicle which precedes plaque formation and inhibit or control the formation of bacterial plaque" (See Ractliff col. 2, lines 29-33; col. 1, lines 20-21; col. 3, lines 50-51; col. 4, lines 18-23, 50-51), nowhere does Ractliff disclose, teach, or contemplate a method for removing plaque.

The Examiner takes the position that it would have been apparent to a skilled person that "compounds that break down the constituents of plaque could be used both for the retardation of plaque growth, and the removal of plaque already present" (See Office Action, page 6). Alternatively, the Examiner asserts that Ractliff inherently discloses a method for removing plaque by virtue of the repeated application of the chlorine dioxide compounds to retard plaque growth.

Applicant respectfully disagrees. The chlorine dioxide of Ractliff prevents and inhibits plaque formation by oxidizing sulphide bonds in sulfated glycoproteins "to inhibit pellicle formation ... Since acquired pellicle is the first step in plaque formation, this initial inhibition alters the sequence of events to follow. The second step, bacterial adhesion and subsequent steps are consequently retarded." (See Ractliff col. 3, lines 54-55; col. 4, lines 6-19). Because the pellicle is composed of a simple coating of glycoproteins whereas plaque is a complex and dense material mass composed of glucans; fructans; dead cells; cell debris; food debris; high molecular weight polymers; altered salivary glycoproteins, proteases, chemotactic and inflammatory inducing substances; and organisms (See Ractliff col. 1, lines 58-68), there is no reason that a skilled person would conclude that the same composition effective for preventing simple pellicle formation would also be effective for removing the complex extracellular matrix that forms plaque or that it would be capable of removing plaque using the same mechanism, i.e. oxidizing glycoproteins.

In addition to inhibiting the deposition of glycoproteins, i.e. pellicle formation, which is a precursor in the formation of plaque, Ractliff also prevents plaque formation by oxidizing compounds in plaque that would otherwise serve as nutrients for bacterial growth (See Ractliff

col. 4, lines 23). Removing the nutrient source for bacterial growth, however, will not remove pre-existing plaque and thus cannot be employed as a plaque removal method.

In response to the Examiner's reliance on the statement that "these biochemical compounds are attacked to a greater or lesser extent by stabilized chlorine dioxide" for teaching that the composition of Ractliff is capable and effective for removing plaque, Applicant respectfully points out that the referenced biochemical compounds (i.e. sulphated glucosamineglycans, proteoglycans, glycoproteins, sugar, proteins, and lipids), are not the only components of the complex extracellular matrix that forms plaque. As discussed at col. 1, lines 58-68, plaque further contains dead cells; cell debris; food debris; high molecular weight polymers; proteases, chemotactic and inflammatory inducing substances; and organisms. Therefore, while Ractliff teaches that chlorine dioxide may oxidize the bacterial nutrient base in plaque, in view of the complex makeup of plaque, a skilled person would not conclude that the composition would also be effective for removing plaque.

According to MPEP §2112.02,

> "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) ... 'To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) ... 'In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.' *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)"

In view of the complex structure of plaque as discussed above, there is no reasonable basis for concluding that the composition of Ractliff would necessarily be effective for removing plaque. Notably, the Examiner has failed to provide any evidentiary proof to substantiate this conclusory assertion. Applicant therefore respectfully asserts that the Examiner has not met his burden of proof in establishing inherency. In the present case, inherency must be established by the Examiner since Ractliff does not actually teach or suggest a method for removal of plaque.

The other cited prior art references also fail to teach a method for removing plaque and therefore do not rectify the deficiency of Ractliff. As previously admitted by the Examiner, "[Hellgren] does not teach or suggest that the composition may be used to treat or remove dental plaque ... [and Karlstam] does not teach the use of the enzyme to degrade plaque" (See page 8 of the Office Action dated January 17, 2008). Notably, the Examiner has not retracted this statement that Hellgren and Karlstam do not teach a method for removing plaque in subsequent Office Actions, including the June 12, 2009 Office Action.

Because the cited references fail to disclose all the elements required by the claims, Applicant respectfully submits that claims 142, 159 and all claims dependent therefrom are not rendered obvious over Ractliff in view of Karlstam and Hellgren.

ii. There is no motivation to combine the cited references

Applicant respectfully submits that there is no motivation to substitute the composition of Ractliff with the krill enzymes of Hellgren and Karlstam as proposed by the Examiner. Col. 3, lines 48 – col. 4, lines 1-23 of Ractliff describes that plaque formation is prevented by reacting stabilized chlorine dioxide with sulphated glycosaminoglycans, prteoglycans, glycoproteins, sugar, proteins and lipids present in the complex extracellular matrix of plaque. In the presence of high oxygen compounds, such as chlorine dioxide, these compounds become unstable and are oxidized. A critical feature of Ractliff is the small size of the chlorine dioxide compound, which enables the chlorine dioxide compound to penetrate the plaque mass in order to reach and react with the aforementioned biochemical compounds therein. By contrast, krill enzymes are substantially larger molecules than chlorine dioxide and thus would be incapable of infiltrating a plaque mass in the manner that chlorine dioxide can penetrate the plaque mass. Consequently, the krill enzymes would not be able to reach the aforementioned biochemical compounds in the same manner as the chlorine dioxide compounds of Ractliff and prevent plaque formation. Accordingly, Applicant respectfully submits that the Examiner's proposal to replace the chlorine dioxide compound of Ractliff with the krill enzymes of Hellgren and Karlstam would render Ractliff inoperable. Pursuant to MPEP §2143.01, "If proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)."

Furthermore, as discussed above, Ractliff prevents plaque formation by oxidizing sulphide bonds of sulphated glycosaminoglycans that form the pellicle and oxidizing select biochemical compounds to remove the nutrient source for bacterial growth. In view of the lack of disclosure regarding the activity of the krill enzymes taught in Karlstam or Hellgren for oxidizing sulphide bonds of sulphated glycosaminoglycans or oxidizing the nutrient source of bacterial growth, a skilled person would have no reason to substitute the krill enzymes of Karlstam or Hellgren for the chlorine dioxide compound in the method of Ractliff as proposed by the Office Action since the mechanism of action of the krill enzymes of Karlstam and Hellgren is completely different than the mechanism of action described in Ractliff.

iii. There is no expectation of success that krill enzymes can effectively remove plaque

Applicant respectfully submits that a skilled person would not expect that the Examiner's proposal to modify the method of Ractliff with the krill enzymes of Hellgren and Karlstam would be effective for removing plaque. Plaque is a complex and dense material mass composed of glucans; fructans; dead cells; cell debris; food debris; high molecular weight polymers; altered salivary glycoproteins, proteases, chemotactic and inflammatory inducing substances; and organisms (See Ractliff col. 1, lines 58-68) as well as sulphated glucosamineglycans, proteoglycans, glycoproteins, sugar, proteins and lipids (See col. 3, lines 65-68 of Ractliff). The aforementioned component categories of plaque can include numerous species of chemical compounds, molecules, and organisms, all of which may be chemically combined and reacted in numerous unpredictable arrangements. Because a skilled artisan recognizes that enzymes have a high degree of specificity for only one type or one related group of molecules, the skilled artisan would know that a single enzyme would not be sufficient to effectively degrade the complex extracellular matrix of dental plaque.

Consequently, the mere fact that the krill derived enzyme of Karlstam is known to degrade the specific glycosaminoglycan, hyaluronic acid, is insufficient to indicate to a skilled person that the krill enzyme would be effective for removing the complex extracellular matrix of dental plaque. First, there is no indication in the record that hyaluronic acid is actually present among the complex matrix of materials that form dental plaque. Thus, a skilled person has no way of knowing whether a krill-derived hyaluronidase, as disclosed in Karlstam would have any effect on dental plaque since dental plaque may not even contain hyaluronic acid.

Further, even if hyaluronic acid were present in dental plaque, degradation of only the hyaluronic acid component of the complex matrix of several materials would not be expected to remove the complex extracellular matrix of dental plaque as required by the present claims. Thus, from the information provided by Karlstam and Ractliff, the skilled person cannot conclude that krill enzymes would be effective for the removal of dental plaque.

Similarly, Hellgren teaches that particular extracts of krill enzymes can be used to clean teeth but does not address plaque removal. Due to the lack of specificity in Hellgren, a skilled person therefore has no basis for concluding that the krill enzyme extracts would be effective for removing dental plaque. Furthermore, the Examiner has not demonstrated that it is known that the specific mixture of exo- and endo-peptidases taught in Hellgren, would have any effectiveness in removing dental plaque. In view of the well known issue of enzyme specificity, as discussed above, the skilled person therefore would not automatically conclude that the limited krill enzyme extracts addressed in Hellgren would be effective for the removal of the complex extracellular matrix of dental plaque which contains numerous materials of different chemical nature.

Accordingly, for these reasons, Applicant respectfully submits that the cited references fail to disclose all the limitations required by the independent claim and that one of ordinary skill in the art would not be motivated to or have any reasonable expectation of success for combining the cited references to achieve removal of the complex extracellular matrix of dental plaque, as required by independent claims 142 and 159. Favorable consideration, withdrawal of the rejection and issuance of a Notice of Allowance are requested.

Date: December 10, 2009

Respectfully submitted,

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Enclosure: Corrected Filing Receipt in U.S. Patent Application No. 09/549,642

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